Ethynylcytidine

Cat. No.: HY-16200

CAS No.: 180300-43-0

Molecular Formula: $C_{11}H_{13}N_3O_5$

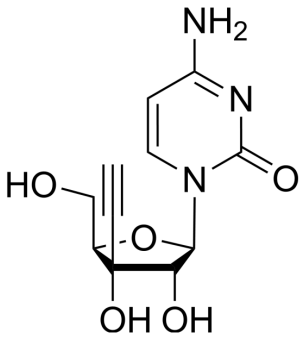
Molecular Weight: 267.24

Target: Nucleoside Antimetabolite/Analog; DNA/RNA Synthesis

Pathway: Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (935.49 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.7420 mL	18.7098 mL	37.4195 mL
	5 mM	0.7484 mL	3.7420 mL	7.4839 mL
	10 mM	0.3742 mL	1.8710 mL	3.7420 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (7.78 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (7.78 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (7.78 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ethynylcytidine (ECyD), a nucleoside analog and a potent inhibitor of RNA synthesis, inhibits RNA polymerases I, II and II. Ethynylcytidine has robust antitumor activity in a wide range of models of cancer[1][2][3]. Ethynylcytidine is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target

nucleoside antimetabolite[1]

In Vitro	The IC_{50} values of Ethynylcytidine in the five human tumors with 4, 24 and 72 h exposure range from 0.114 to 1.032 μM, 0.015 to 0.067 μM, and 0.008 to 0.058 μM, respectively. These results suggest that the cytotoxicity of Ethynylcytidine tends to become stronger as the exposure time becomes longer. The differences in IC_{50} values between the 24 and 72 h exposure times are not large, and Ethynylcytidine appeares to show sufficiently potent cytotoxicity at the 24 h exposure time in all 5 human tumors. Even at the 4 h exposure time, Ethynylcytidine clearly shows potent cytotoxicity with IC_{50} values at submicromolar concentrations in 4 of the 5 human tumors[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In both OCUM-2MD3 and LX-1 xenografts, tumor regression is noted and a very potent antitumor effect with an tumor growth inhibition rate (IR) on day 15 of approximately 90% or even higher is observed at the minimum toxic doses of Ethynylcytidine (TAS-106) on all three administration schedules. In particular, administration of Ethynylcytidine at 6 mg/kg once weekly exhibits a marked tumor shrinking effect with an IR of 98% against the LX-1 tumor. While Ethynylcytidine treatment on an either 3 or 5 times weekly schedule has a potent antitumor effect with an IR of approximately 85%, the IR of Ethynylcytidine once weekly is less than 60% and its antitumor effect is rather weak[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	MIAPaCa-2 cells are maintained in Dulbecco's modified Eagle's medium supplemented with 10% FCS and 2.5% horse serum. Cells in the exponential growth phase are seeded onto 6-well plates (5×10^4 cells/1.8 mL/well) on day 0. Twenty-four hours after seeding, on day 1, Ethynylcytidine (TAS-106) (6 concentrations range from 0 to 100 μM) is added to cultured cells (3 wells at each concentration) at a volume of 0.2 mL/well. After 4 and 24 h, on the 4 and 24 h Ethynylcytidine exposure schedules, the drug-containing medium is removed, and the cells are washed twice with Dulbecco's phosphate buffered saline and subsequently cultured in drug-free medium until day 4. On the 72 h exposure schedule, after adding the Ethynylcytidine, cells are cultured continuously until day 4. On day 4, cell numbers are determined and converted to values related to the cell numbers on day 1. The concentration of Ethynylcytidine which inhibits cell growth by 50% (IC_{50}) is calculated from this relative cell growth. Two or three individual experiments are conducted on each cell line to confirm reproducibility[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Nude rats s.c. transplanted with LX-1 human lung tumors are given a single i.v. dose of [^{3}H]Ethynylcytidine (TAS-106) (6 mg/kg, 3.7 MBq/kg). For analysis of the distribution of radioactivity and intratumoral Ethynylcytidine metabolism, serum and various tissues (tumor, skin, lung, liver, kidney, spleen, small intestine, large intestine, testis, brain, and bone marrow cells) are sampled from 3 rats at each of the following 6 time points: 0.5, 1, 2, 4, 8 and 24 h after i.v. administration. At each point in time, bone marrow cells are collected from the 3 rats and combined into a cell pellet. All samples of serum, bone marrow cell pellets, and tissues are immediately frozen on dry ice and stored at -30°C until used[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Shimamoto Y, et al. Antitumor activity and pharmacokinetics of TAS-106, 1-(3-C-ethynyl-beta-D-ribo-pentofuranosyl)cytosine. Jpn J Cancer Res. 2001 Mar;92(3):343-51.

[2]. Abdelrahim M, et al. TAS-106: preclinical, clinical and beyond. Oncology. 2013;85(6):356-363.

[3]. Hammond-Thelin LA, et al. Phase I and pharmacokinetic study of 3'-C-ethynylcytidine (TAS-106), an inhibitor of RNA polymerase I, II and III,in patients with advanced solid malignancies. Invest New Drugs. 2012;30(1):316-326.

Caution: Product has not been fully validated for medical applications. For research use only.

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